UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/606,222	06/29/2000	Kirk R. Thomas	2323-139-II	7631

6449 7590 11/26/2002

ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/606,222	Applicant(s) THOMAS ET AL.	
	Examiner Thaian N. Ton	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6/18/02 .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6,20-24,32 and 38-42 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6,20-24,32 and 38-42 is/are rejected.

7)☒ Claim(s) 32 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 29 June 2002 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request filed on 9/11/02 for a Request for Continued Examination (RCE) under 37 CFR 1.114 is acceptable and a RCE has been established. An action on the RCE follows.

Applicants' Amendment, filed 6/12/02 has been entered. Claims 7-19, 25-31 and 33-37 have been cancelled. Claims 1, 2, 5, 6, 24 and 32 have been amended. Claims 38-42 have been added.

Claims 1-6, 20-24, 32 and 38-42 are pending and under current examination.

Any rejection made of record in the prior Office action, mailed 3/12/02, Paper No. 12, and not made of record in the instant Office action, has been withdrawn in view of Applicants' arguments and/or amendments to the claims.

Claim Objections

Claim 32 is objected to because of the following informalities: the claim refers to "the method" of claim 20, however, claim 20 is a nucleic acid molecule. Appropriate correction is required.

Drawings

Applicant(s) is/are hereby notified that the required timing for correction of drawings has changed. See the last 6 lines on the sheet, which is attached, entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". Due to the above notification

Applicant(s) is/are required to submit drawing corrections with the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The prior rejection of claims 1-6, and newly added claims 38-42 under 35 U.S.C. 112, first paragraph, is maintained for reasons advanced on pages 2-7 of the prior Office Action.

The specification, while being enabling for a method for deleting a nucleic acid sequence in a specified tissue of a mouse from a DNA molecule introduced into the mouse, comprising introducing a DNA molecule which comprises a recombinase site, a tissue-specific promoter, a recombinase gene, a foreign DNA and a recombinase site, the specification does not reasonably provide enablement for a method for deleting a nucleic acid sequence in a specified tissue of organisms, to the breadth claimed, from a DNA introduced into the organism, comprising introducing a DNA molecule which comprises a recombinase site, a tissue-specific promoter, a recombinase gene, a foreign DNA and a recombinase site, the growing of organisms,

to the breadth claimed, so that the tissue-specific promoter is active for expression of the recombinase gene in the specific tissue, and where the foreign DNA is deleted in the specified tissue during growth of organisms to the breadth claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants argue that the claims have been amended to recite a method for deleting a nucleic acid sequence from a DNA molecule that has been introduced into a cell, whereby the sequence is deleted in a regulatable manner using a regulatable promoter, which is supported by the specification. [See p. 4, 3¶ of the Response]. Applicants argue that this amendment overcomes the prior enablement rejection, which is directed to the specification's lack of teaching to show introduction of DNA into ES cells for other than mice is unpredictable, and that the claims prior to amendment, encompass the use of stem cells and transgenic animals from other than mice.

Applicants' arguments have been considered, however, they are not found persuasive. In response, it is noted that although the independent claims have now been amended to recite "an animal cell" [see line 2 of claim 1], the claims encompass an animal cell, both *in vitro* and *in vivo*. Indeed, further dependent claims recite that the cell is part of a tissue [see claim 39]. As such, the prior rejection is maintained that the claimed invention encompasses on the deletion of nucleic acid

sequences from a DNA molecule that has been introduced into an organism. As Applicants have stated in the prior Response, the claimed invention is not directed to the generation of a transgenic animal; however, certain embodiments of the present invention require the use of a transgenic animal. As such, it is reiterated that the state of the art of producing transgenic animals is unpredictable, as evidenced by Moreadith *et al.* and Mullins *et al.* (see the Office action dated 6/20/02, p. 6-7). A demonstration has not been provided by the specification or the prior or post-filing art with regard to the generation of any species of animal ES cells, other than the mouse, which can give rise to the germline tissue of a developing animal. As such, the Examiner maintains that ES cells are elements essential to certain embodiments of the claimed invention.

Applicants argue, with regard to the prior Office action's opinion that some of the claims are directed to gene therapy, or use in gene therapy, are not enabled, that the relevant claims have been amended or cancelled to recite molecules or methods for deleting a nucleic acid of interest from a cell, and that the specification clearly shows how to make and use the presently claimed invention, including the presentation of experimental details and results, and Applicants reiterate that it is not necessary to introduce the DNA constructs into ES cells for the invention to work [see pp. 4-5, bridging ¶].

In response, it is noted that although the claims, as amended, now recite "an animal cell", certain embodiments of the claims encompass germ-line modification.

For example, claim 42 recites that the tissue which the cell is part of is male or female gametic tissue, which encompass germ-line gene therapy. The unpredictable state of the art of germ-line gene therapy is presented in the Office action sent 6/20/01, p. 7. Furthermore, it is noted that the instant specification discusses various applications of the claimed methods, such as the generation of knockout animals for the removal of a marker gene, the generation of mice harboring conditional-mutant alleles, and as *in utero* human gene therapy [see pp. 7-8 of the instant specification]. These contemplated applications encompass the use of ES cells [in first two instances] and germ-line gene therapy. Although the claims have been amended to recite molecules or methods for deleting a nucleic acid of interest from a cell, wherein the deleted nucleic acid comprises a wild-type allele or a fragment thereof of a gene, the specification fails to provide teachings or guidance for any other enabled use for the claimed method that does not encompass utilizing ES cells, or germ-line gene therapy.

Applicants argue that the Examiner has not specified an independent basis for rejection claim 20 and the claims, which depend therefrom for lack of enablement. Applicants' arguments are found persuasive and the rejection of claims 20-24 and 32 is withdrawn.

Accordingly, in view of the quantity of experimentation necessary to determine the parameters listed above for achieving a method for deleting a nucleic acid sequence in the specified tissue of an organism, the lack of direction or

guidance provided in the specification for the isolation of animal ES cells from any species, other than that of the mouse, as well as the unpredictable and undeveloped state of the art for the isolation of animal ES cells from species other than mice, as well as the claimed breadth of the claims, encompassing the use of ES cells from any particular organism for the generation of any particular type of organism, the lack of guidance and direction provided by the specification to carry out gene therapy as broadly claimed, involving any particular type of target cell, route of administration and subject, and the unpredictable and undeveloped art of gene therapy, it would have required undue experimentation for one skilled in the art to carry out the claimed methods, nucleic acid constructs, and methods of using the same.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20, as written, is unclear. The claim recites a nucleic acid molecule comprising a recombinase site, a tissue-specific promoter, a recombinase gene, a foreign DNA and a recombinase site. However, the claim does not limit the order in which these components could be assembled. It is suggested that the claims recite that these components are operably linked. Claims 21-24 and 32 depend from claim 20.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (703) 305-1019. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Tiffiany Tabb, Patent Analyst, at (703) 605-1238. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Deborah Crouch

TNT
Thaian N. Ton
Patent Examiner
Group 1632

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP ~~1800~~ 1630